Knowledge Acquisition Session Report

Session Date: March 1, 2000 **Time:** 9:00-11:00a.m.

Session Topic: DCP Protocol Information Office

Knowledge Analysts: Lisa Chatterjee, Oracle; Bill McCurry, Robert Harding, ScenPro, Inc.

Organization: NCI Division of Cancer Prevention, Protocol Information Office

Session Location: PIO Offices, EPN Building, Rockville, MD.

Type of Session:

X Interview _____ Task Analysis _____ Scenario Analysis
____ Concept Analysis _____ Observation _____ Structured Interview
____ Other:

Documentation: KA Session Report

Documents Provided by Linda Parreco
-DCP PIO: Development Plan.
-Protocol Review Process.
-Protocol Review Criteria by Section.
-CCSA Internal Protocol Review Process.
-PIO: Proposed Protocol Review Process.
-Phase II Solicitation Process: protocol Review.
-Attachment A: Types of protocols for which the DCP Protocol Information Office Will Coordinate Reviews.
-A Phase 2 Protocol: Celecoxib UV 1999.
-DCP PIO: Request for Concept/ Protocol Review

Documents Provided by Anita Lomonico
-Approval
-Request to outside reviewer to participate in a review.
-Response to protocol review.
-CC Research Checklist
-Contract Status
-Protocol Complete Sheet
-Protocol Concept Tracking
-Protocol Document 1: "University of Rochester Cancer Center, CCOP Research Base. URCC U4599, NCI U4599"
-Protocol Transfer Document
-Appendices A: "Study Parameters: Baseline and Follow-up Evaluations"
-Appendices B: "Eligibility Checklist and On Study Form"
-Appendices C: "Model Consent Form"
-Appendices E: "Instructions For Self-Administering"
-Appendices F: "Off Treatment Notice"
-Appendices G: "MedWatch Form"
-Appendices H: "FACT-G"
-CSS
-Request for Applications for Cooperative Agreements

General Topic Area

PIO (Protocol Information Office) interaction with DCP (Division of Cancer Prevention) research groups.

Session Objectives

- Obtain a detailed understanding of the PIO's day-to-day tasks and their associated information needs.
- Produce detailed process analysis representations.

Report Summary

This report focuses on the daily tasks and information needs of the Protocol Information Office (PIO) in the National Cancer Institute's Division of Cancer Prevention (DCP). The DCP is dedicated to cancer prevention research, and the PIO supports this by coordinating the administration of all documents related to DCP research studies. The PIO consists of two people, Linda Parreco (PIO Head) and Jennifer Flach (PIO Specialist). Ms. Parreco and Ms. Flach administer two similar but distinct research study processes within DCP. One process supports cooperative group studies managed by DCP's Community Clinical Oncology Program (CCOP), while the other process supports contract studies managed by DCP's Organ System Research Groups (OSRG). The PIO has established a goal of developing one process that will support both types of research studies.

Division of Cancer Prevention Overview

The Division of Cancer Prevention (DCP) is one of eight Divisions within the National Cancer Institute (NCI). Although other NCI divisions manage clinical research studies, DCP is responsible for managing research studies related to cancer prevention.

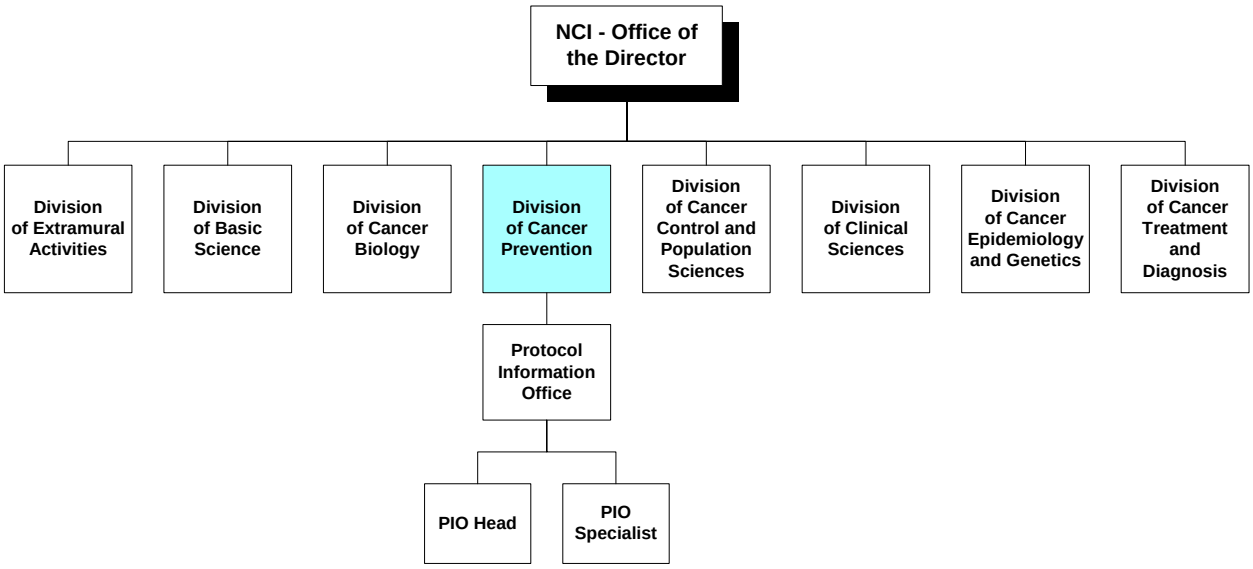


Figure 1. Organization Chart for Division of Cancer Prevention and its Protocol Information Office

Prior to 1999, the NCI's Division of Cancer Prevention and Control (DCPC) managed cancer prevention research. NCI reorganized in 1999, dividing the DCPC into two separate divisions: 1) Division of Cancer Control and Population Studies (DCCPS), and 2) the Division of Cancer Prevention (DCP). The DCP is dedicated to cancer prevention research projects including chemoprevention, nutritional science, genetics, infectious agents, early detection studies, quality of life, and cancer symptom management for the National Institute of Health (NIH).

The following diagram shows the various research groups within the DCP. The PIO interacts with the highlighted groups in its efforts to coordinate and administer research studies.

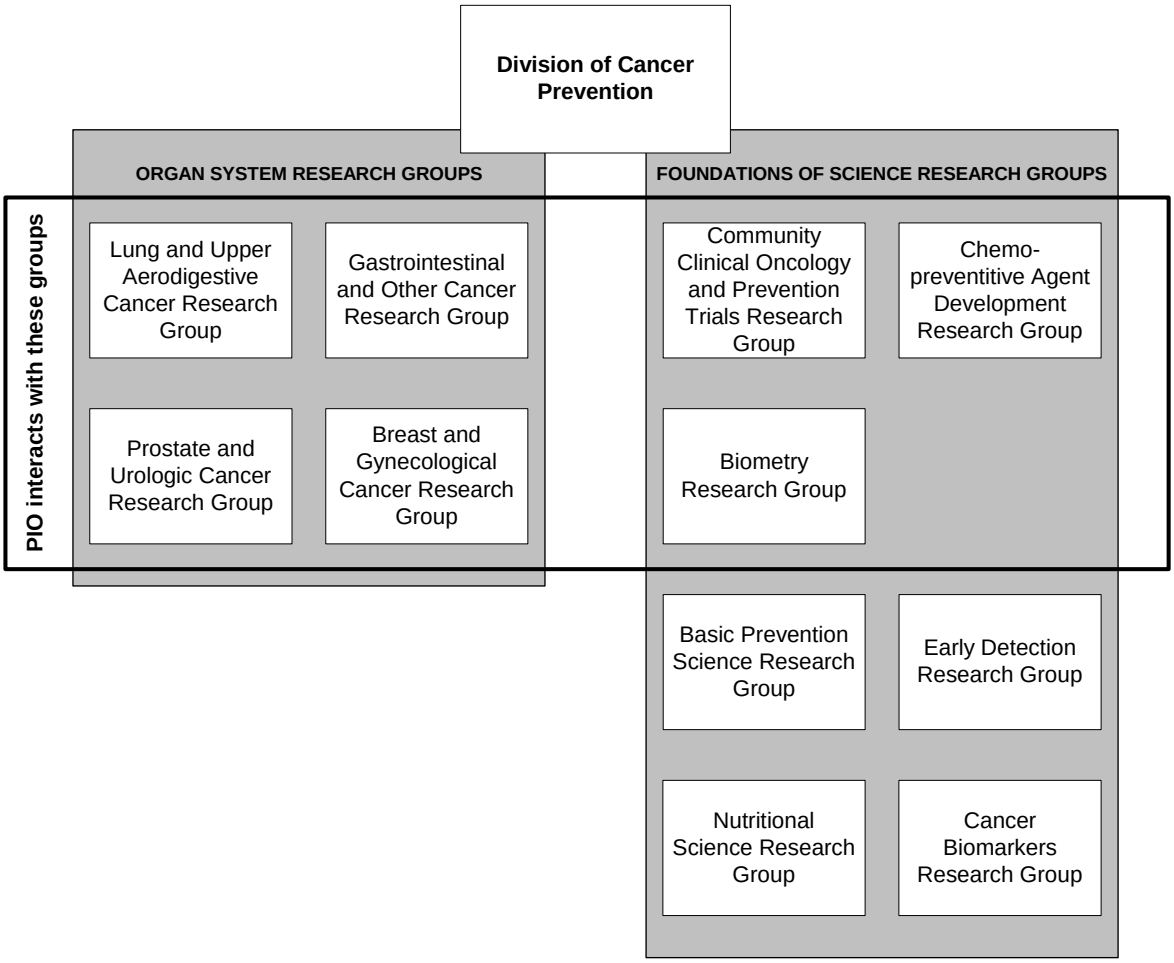


Figure 2. DCP Research Groups That Interact With the Protocol Information Office

The PIO regularly interacts with seven of the DCP's eleven research groups. The four Organ System Research Groups (OSRG) focus on organ site-targeted research studies, and they primarily manage studies resulting from contracts between NCI and cancer research centers. The Foundations of Science Research Groups focus on scientific aspects of cancer prevention. One of these groups, the Community Clinical Oncology and Prevention Trials Research Group (CCOP) manages studies resulting from cooperative agreements between NCI and CCOP research bases. The Biometry Research Group provides statistical expertise required for the evaluation of proposed studies, and the Chemopreventitive Agent Development Research Group manages the chemical agents involved in cancer prevention research studies.

The DCP is organized into a matrix structure inspired by the Biotech industry. This structure is comprised of two main research 'arms'. One is made up of seven sub-groups, each of which specializes in a different scientific aspect of cancer prevention research. The other 'arm' is devoted to organ site-targeted research and has four sub-groups reflecting different target organ sites.

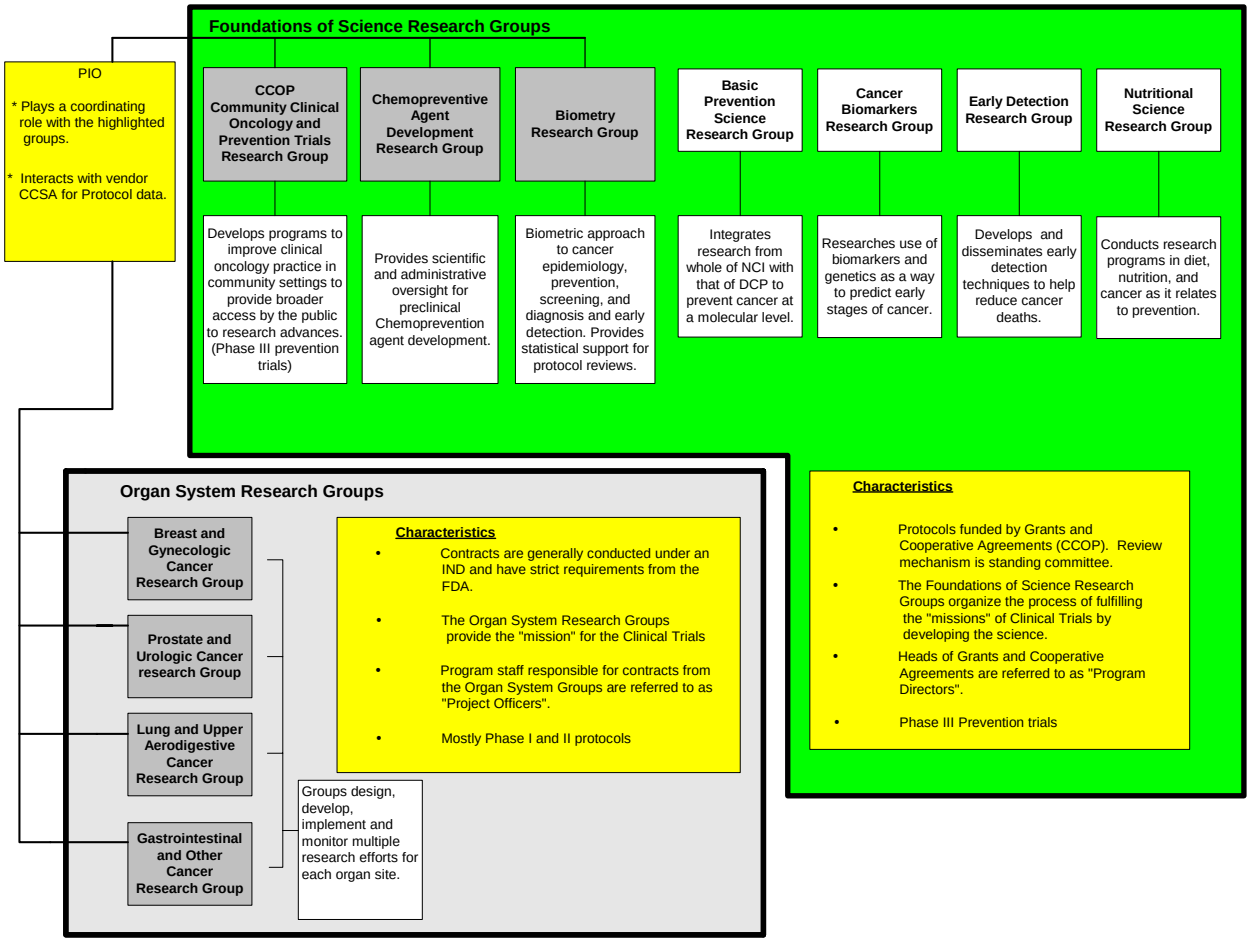


Figure 3. DCP Matrix Structure and Interaction with the Protocol Information Office

The Protocol Information Office personnel interact with the DCP Research Groups to coordinate and administer the documentation for DCP research studies. These interactions include both formal and informal communication with OSRG project officers, CCOP program directors, review board members, and review board chairpersons.

PIO Overview

The PIO coordinates the administration and tracking of documents and correspondence for DCP cancer prevention research studies. DCP research studies follow a general sequence of administrative steps, and the PIO's coordination efforts follow that sequence. The figure below illustrates the major steps for a DCP study.

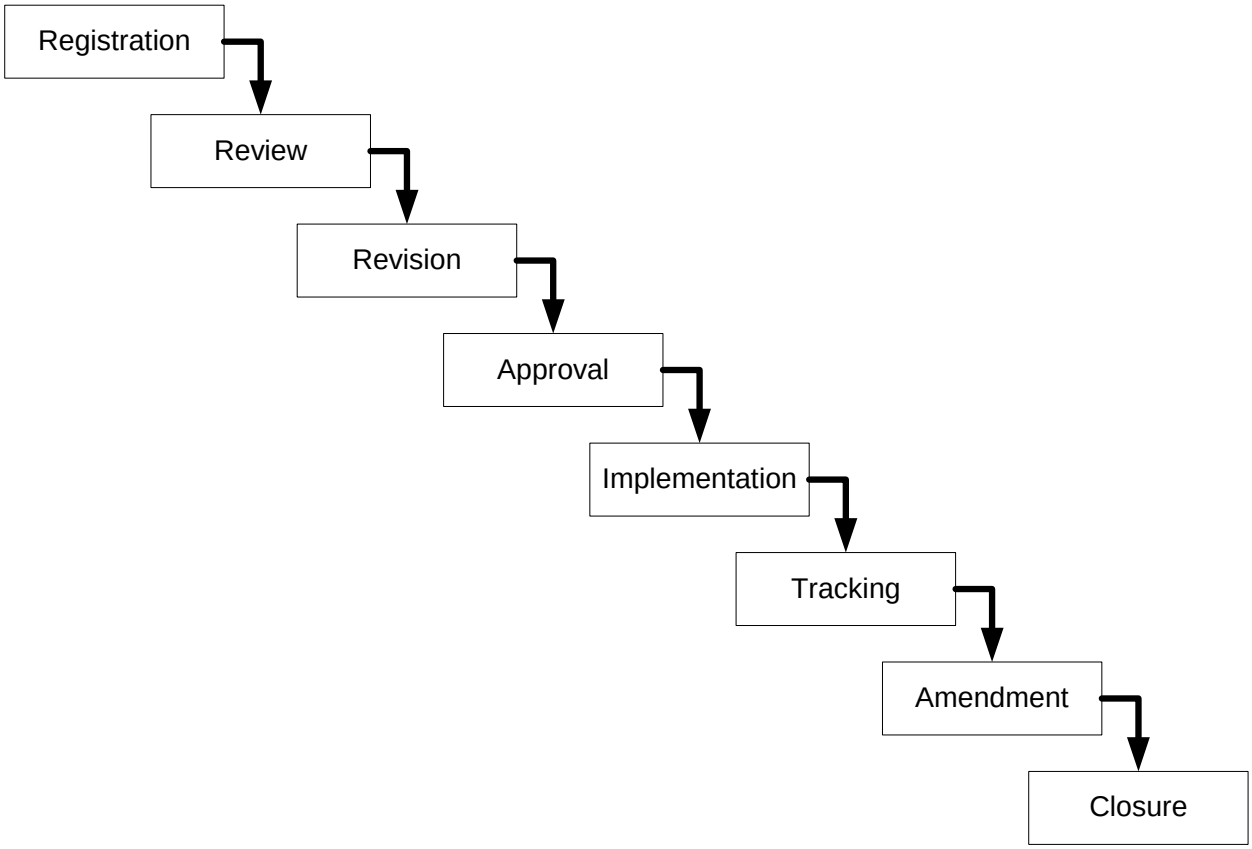


Figure 4: Major Steps in Administration of a DCP Research Study

The details of these steps may vary according to the type of research study, but most studies will follow this sequence of major steps. Many of the PIO's tasks can be associated with a particular step in this sequence.

PIO Tasks

The PIO's primary tasks are (1) to coordinate the administration of study-related documents for the DCP, and (2) to track and maintain correspondence related to DCP studies. The following figure illustrates these primary tasks and the sub-tasks that fall under them.

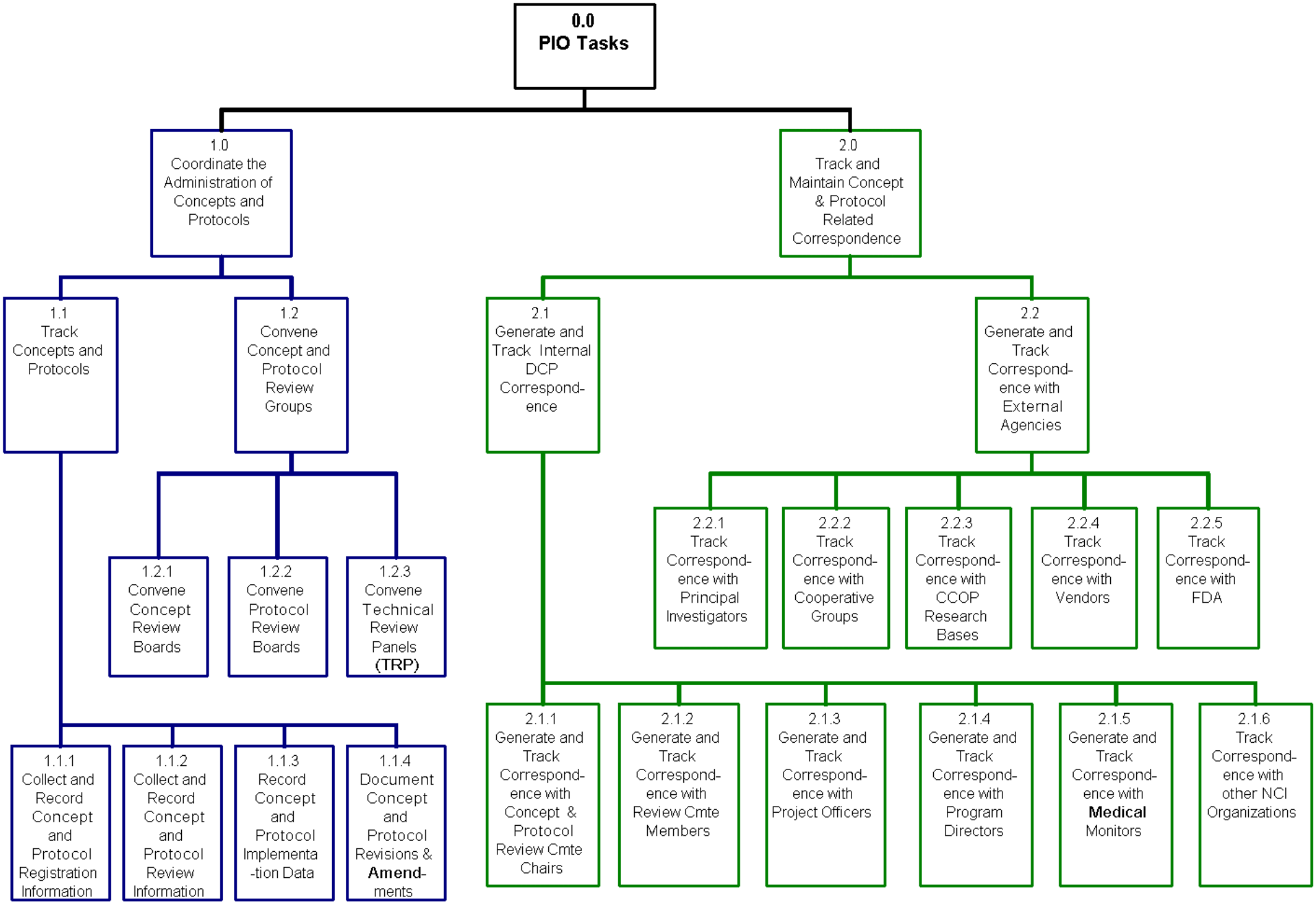


Figure 5 - DCP PIO Task Hierarchy

1.0 Coordinate the Administration of Concepts and Protocols
Protocol Information Office coordinates the tracking and administration of all DCP research studies funded by contracts (in the case of OSRG) and cooperative agreements (in the case of CCOP). Concepts are brief (10 page) documents that describe a proposed study in a general fashion. Protocols are detailed documents that specifically describe how a study will be conducted.

1.1 Track Concepts and Protocols
Protocol Information Office collects, organizes, and reports on concept and protocol data. This includes registration data, information needed to review a concept or protocol, implementation information such as patient accruals, protocol revisions and amendments, and study closure information.

1.2 Convene Concept and Protocol Review Groups
Protocol Information Office organizes and schedules Concept Review Boards, Protocol Review Boards, and Technical Review Panels. This includes locating board or panel members with the expertise appropriate to a particular study.

2.0 Track and Maintain Concept and Protocol Related Correspondence
Protocol Information Office generates and tracks study-related correspondence with other areas of DCP and with external agencies or groups. This correspondence is frequently driven by PIO's coordination activities, such as correspondence with review board members that is needed in order to convene a review board.

2.1 Generate and Track Internal DCP Correspondence
Protocol Information Office handles all protocol and concept related correspondence within DCP. In this capacity, PIO corresponds with OSRG project officers, CCOP program directors, medical monitors, review board members, and review board chairpersons.

2.2 Generate and Track Correspondence With External Agencies
PIO tracks all protocol and concept related correspondence with external agencies. This includes the principal investigators for studies, cooperative groups, CCOP research bases, vendors, and the FDA.

PIO Concept and Protocol Review Coordination

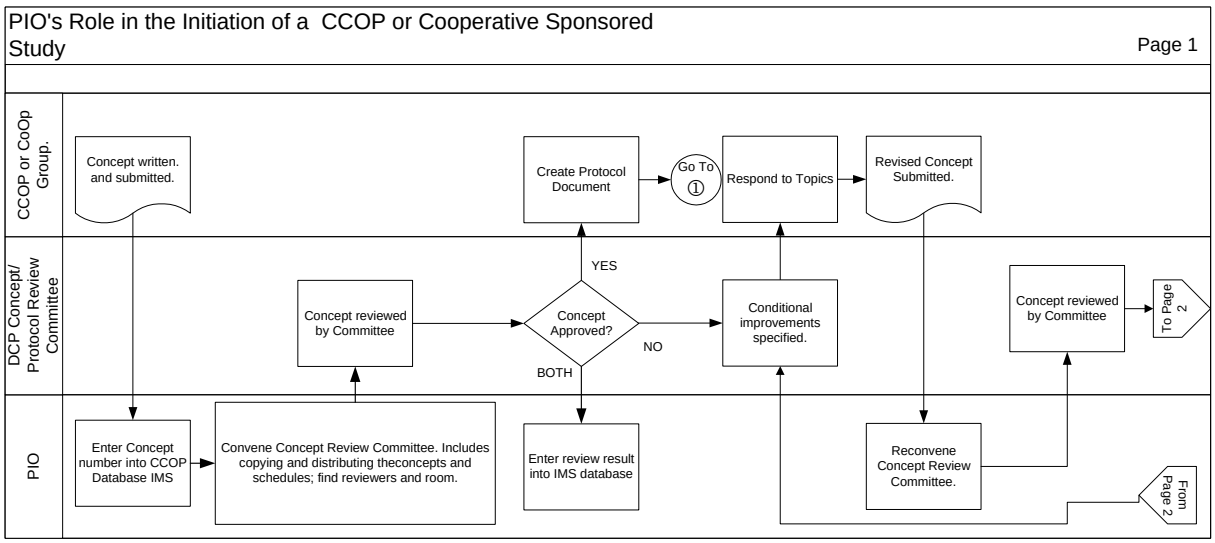
The PIO will coordinate concept and protocol reviews for the following types of studies:

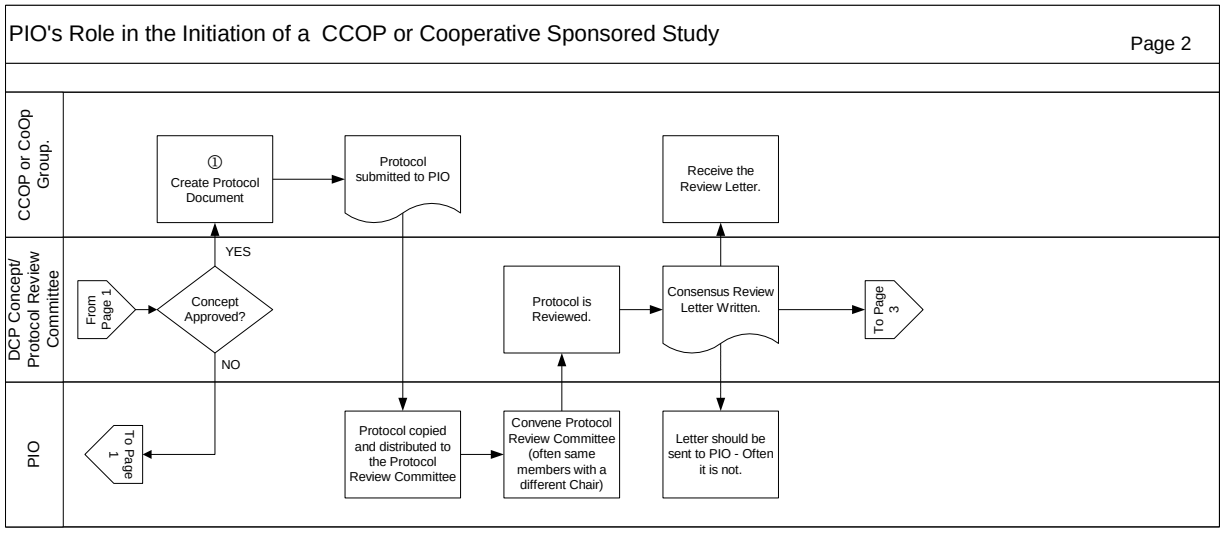
- DCP-sponsored phase I, II, or III human clinical trials
- DCP-sponsored tissue studies
- Traditional research grants or studies not sponsored by NCI, but that use agents for which NCI holds the Investigational New Drug (IND) or controls the drug supply
- Studies in the following scientific areas: chemoprevention, biomarkers, early detection, quality of life, or symptom prevention and control
- Other traditional research grants upon the request of the Program Director

PIO coordinates the administration of two distinct study review processes: (1) CCOP cooperative agreement concepts and protocols, and (2) OSRG contract protocols. A major goal of the DCP Protocol Information Office is to create one set of standard protocol review procedures that will support both study types.

Community Clinical Oncology Program (CCOP) Studies Concept and Protocol Review Process

The PIO manages Community Clinical Oncology Program (CCOP) concepts and protocols as one of its primary responsibilities. The following diagrams illustrate the CCOP concept and protocol review process.





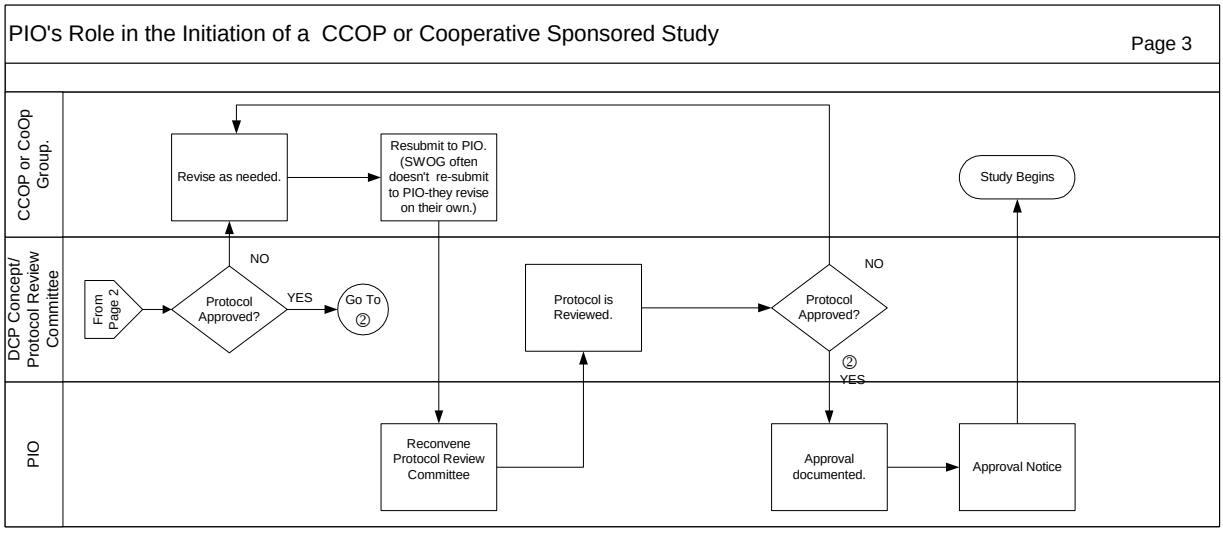


Figure 6: The CCOP Studies Review and Approval Process

CCOP Concept Review and Approval
The review of CCOP studies begins with a document called a Concept. A Concept is a ten-page overview of a proposed study. Concepts are received from CCOP Research Bases, including Cooperative Groups, the University of Rochester, MD Anderson, and Wake Forest. Concepts are reviewed by the Cancer Prevention and Control Concept Review Committee, which is convened by PIO. The committee may approve the concept, reject it, or request improvements. The Concept Review Committee Chair is responsible for responding to the study investigators.

CCOP Protocol Submission
Once a Concept is approved, the investigators prepare and submit a Protocol. A protocol is a lengthy document that describes in detail the methodology that will be used to conduct a study. CCOP program directors review protocols and advise investigators on protocol development prior to the formal review meeting. The investigators submit their protocol to a Protocol Review Committee (PRC), convened by the PIO. Protocol review committee members include a statistical reviewer and a consent form reviewer, and may require outside reviewers for specialty areas.

CCOP Protocol Review and Approval
PIO prefers that reviewers attend the review meeting in person. Reviewers are asked to submit written summaries of their recommendations to the PIO prior to the meeting. However, reviewers generally bring their summaries to the review meeting rather than turning the review summary into the PIO prior to the meeting. The review committee may approve the protocol, reject it, or request revisions. Once a protocol is approved, it may be implemented.

Contract Studies
Protocol Review and Approval Process

The process for Contract Protocol review and approval is more formalized and more clearly defined than the CCOP approval process. This is because Contract studies are generally conducted under and Investigational New Drug and have strict requirements placed on them by the FDA. Therefore, the required Protocol content is well defined.

Contract Request for Proposal
DCP Organ Systems Research Groups initiate the contract process by publishing a Request for Proposals (RFP). This is usually done once or twice a year. The RFP is the mechanism OSRG uses to outline the mission for a particular clinical trial, and is distributed to a pre-approved list of Master Agreement Holders (MAH).

The diagram below depicts the PIO's role in the Contract review and approval process.

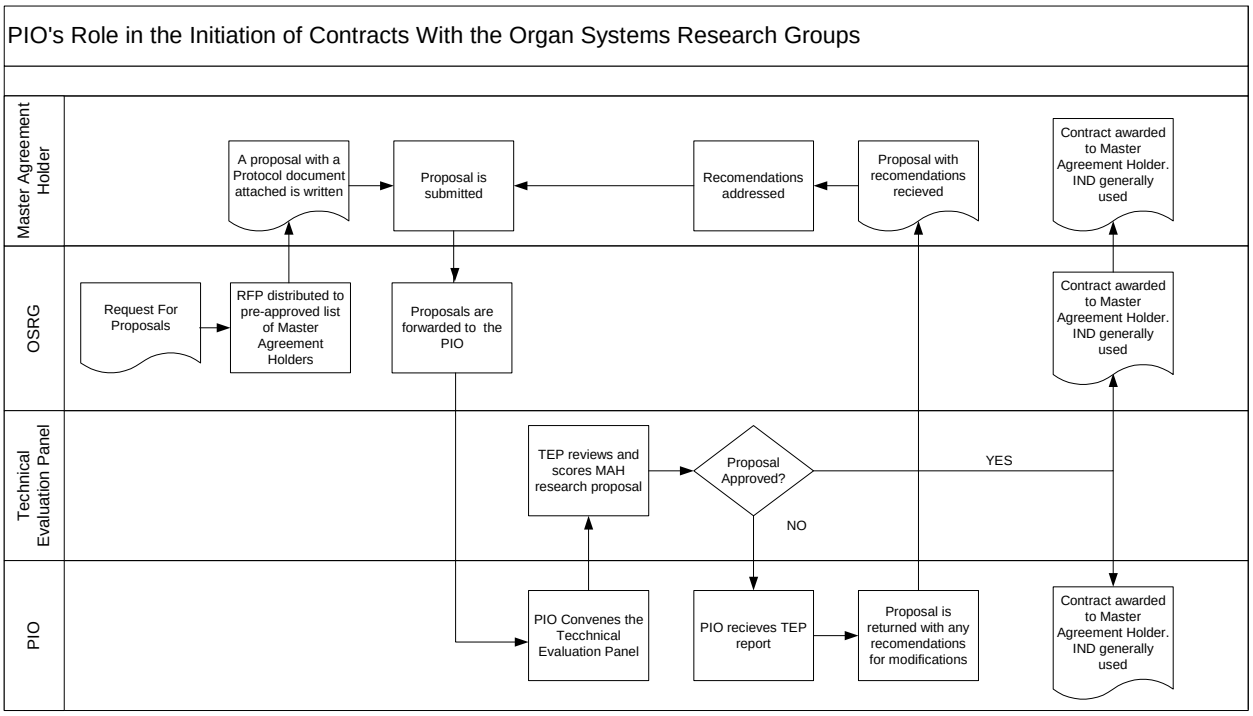


Figure 7: The Contract Studies Review and Approval Process

Contract Proposal Solicitation and Submission

The Organ Systems Research Groups send Requests for Proposal (RFP) to Master Agreement Holders (MAH). Those who are interested write a proposal in response to one or more work statements in the RFP. The proposal includes a clinical trial Protocol. There is no Concept document in the Contract studies review and approval process.

Contract Proposal Review and Approval Process

Proposals and their accompanying Protocols are reviewed and scored by a DCP Technical Evaluation Panel (TEP). The PIO is responsible for convening the TEP and acts as an administrative support entity for TEP functions. The TEP selects institutions from the Master Agreement Holder to award contracts for the specified research. The MAH will be required to modify the Protocol in response to the TEP's recommendations. It will then submit a Protocol Draft Final to the PIO for the next review cycle. This process generally takes one month.

Contract studies (Chemoprevention studies in particular) are conducted under an IND (FDA Form 1572). CCOP investigators are required to have an approved IND prior to initiating a CCOP study.

Contract Study Tracking

The Organ System Research Groups are responsible for monitoring contract-funded research. OSRT project officers interact with principal investigators, vendors, pharmaceutical companies and the PIO in tracking the progress of Contract studies. Study accrual information is reported through the CDUS system. Both PIO and project officer signatures are required on all Protocol-related correspondence for Contract studies.

Contract Study Funding Mechanisms
CCOP studies are supported by grants or cooperative agreements for research bases. A U10 cooperative agreement is used for infrastructure/large dollar amount projects. U19 is used for outside specific research, usually a smaller dollar amount. Both are similar to grants, but the NCI has significant input to the process.

Comparison of the CCOP Studies and Contract Studies Review and Approval Processes

Although similar in sequence, the CCOP study review process and the Contract study review process differ in a number of areas. The table below briefly describes how the two processes compare in each of the major steps for a DCP study.

Major Step	**CCOP Studies Process**	**Contract Studies Process**
Registration	CCOP Research Bases submit Concept Documents	OSRG sends out RFPs; Master Agreement Holders submit proposals that include full Protocols
Review	**Concept**: Reviewed by Cancer Prevention and Control Concept Review Committee **Protocol:** Reviewed by Protocol Review Committee	**Concept:** N/A (no Concept document) **Protocol:** Reviewed and scored by Technical Evaluation Panel
Revision	**Concept:** Investigator may be asked to revise the Concept document, or to incorporate revisions into the Protocol **Protocol:** Investigator may be asked to revise the Protocol.	**Protocol:** MAH modifies Protocol in response to TEP recommendations, then resubmits for next review cycle
Approval	**Concept:** Approved by Cancer Prevention and Control Concept Review Committee (Chair responsible for response letter) **Protocol:** Approved by Protocol Review Committee	**Protocol:** Contract awarded by TEP
Implementation	*Requires additional KA*	*Requires additional KA*
Tracking	Accrual information for ongoing studies is reported through CDUS	OSRG responsible for tracking and reporting ongoing study data. Vendor (CCS Associates) collects and reports the information quarterly
Amendment	*Requires additional KA*	*Requires additional KA*
Closure	*Requires additional KA*	*Requires additional KA*

Vendor Involvement in Concept and Protocol Reviews

Clinical Chemoprevention Study Associates (CCS) is a California-based vendor that provides DCP with IND application and Protocol monitoring services. PIO personnel interact with CCS personnel on a daily basis, typically to request study-related information from CCS. CCS has added a staff member whose primary responsibility is to be liaison to the PIO.

CCS maintains a staff of auditors who perform site visits and collect patient accrual information for research studies. CCS gathers patient-level accrual information and reports the study accrual data to the DCP project officers and to PIO. CCS is required to submit this data on either a quarterly or annual basis, according to the terms of the specific contract.

CCS also provides services in the areas of drug supply management and drug regulatory review. CCS Associates is involved in the process of managing clinical trial drug supplies for some studies. CCS also conducts scientific regulatory reviews of Protocols, tracks amendments sent to the FDA, tracks FDA approvals, and tracks IRB contract approvals.

Current DCP Data Sources

PIO currently has three electronic sources of study data available to them.

1. CCS Associates: CCS uses this database to manage study data for its work with DCP. Some of this data is utilized by the PIO for concept and protocol reviews. Linda Parreco noted that some of the historical data contained in this database would be useful if mapped to the new PIO informatics system. PIO personnel do not currently have 'hands-on' access to this database.
2. IMS DB: This is an in-house tracking mechanism for CCOP.
3. Cynthia Whitman (DCP/COPTRG 301-496-8541) is responsible for CCOP administrative and financial reporting. She has created a database to assist her in this task. This database is related to the IMS database.

PIO Vision

The following is a list of goals for the DCP PIO:

- Develop a consistent standardized process for all protocol and concept reviews.
- Improve the CCOP concept and protocol review guidelines to facilitate valid review and approval decisions.
- Ability to track Investigational New Drug (IND) number and sponsor name.
- Generate an expert reviewer pool database to facilitate the concept and protocol review process.
    - Track reviewer's schedules, roles, and training.
    - Record who has completed reviews. (How many, review type, and the duration of the review)
    - Provide a listing of doctors to support media queries.
- Facilitate the electronic submission of Protocols.
- Improve the timeliness and quality of the protocol review and tracking process.
- Ability to generate a consensus report and cover letter to the Primary Investigator (PI).

- Develop tools to communicate effectively with PIs and cooperative groups.
- Develop an efficient and effective technology-enhanced mechanism for handling protocol revision and amendment review processes.

System Requirements

Following is a list of system requirements provided by DCP PIO personnel:

HIGH PRIORITY

- Track each step of concept and protocol review and administration process, including:
    - Arrival
    - Abstract
    - Agents and/or interventions
    - Reviewers names; date review expected; date review provided
    - Reviews scheduled; date reviewer comments due back to DCP PIO; actual date received; date PIO letter due out; actual date out
    - Review outcomes
    - Protocol revisions: date revised protocol requested from PI; actual date received from PI
    - Amendments process
    - Number and rate of expected subject accrual
    - Study initiation date
    - Expected study completion date; date that study will finish given the current rate of accrual
- Provide IND and holder information.
- Provide consistent protocol numbering system.
- Provide clarity with CTEP around definition of cancer prevention, control.
- Include process for QA on data entered.
- Allow continuous quality.
    - Improvement activities:
        1. Make graphs to PIO turnaround times(?).
        2. Tools to measure performance.
- Define requirements for complete concept/ protocol.
- Standardize categories for approval/ disapproval.
- Flag "languishing" studies. Need quarterly print-out for project officers to show which studies have accrual less than the expected rate

MEDIUM PRIORITY

- Track the lapsed time between each step of review process.
- Create a "reviewer pool" containing possible reviewers with specialty area and contract information. Categorize according to Branch/Title and specialty area
- Integrate relevant pieces of legacy systems.
- Integrate with current CTEP process.
- Send updates to PDQ.
- Incorporate CDEs
    - Approved

    - Relevant
- Provide ad hoc query for end users.
- Create the review schedule and documents for distribution.
- Allow users to see where protocol is in approval process (internal & external users)
- Put timelines on required actions – Track progress against timelines.
- Provide tracking of FDA submissions.
- Inform the agent decision committee.
- List of concepts and protocols under review
- List of approved protocols

LOW PRIORITY

- Template or process for compiling Consensus Review Letter.
- Method for online review/ edit of documents by multiple reviewers.
- Templates for other document types i.e. Approval letters etc.
- Common calendar for scheduling review meeting.
- Tools for Primary Investigators to put together concept and protocol documents.
- Process for electronic review of concepts and protocols against a 'criteria' tool.
- Electronic submission of PI documentation.
- Link with CDUS-type system to connect protocol tracking with results.
- Web-based Investigators Handbook
- Web-based RFA forms and tables
- Web-based FAQ's about concept and protocol development and submission process

Entries for Domain Dictionary

CCOP (Community Clinical Oncology Program): One of the Foundations of Science Research Groups within the Division of Cancer Prevention (DCP) responsible for managing clinical studies resulting from agreements between the NCI and CCOP research bases.

CCS (Clinical Chemoprevention Study Associates): a California-based vendor that provides the DCP with IND application and protocol monitoring services.

Concept: A ten page overview of a proposed cancer research study. Usually submitted for CCOP related studies.

DCP (Division of Cancer Prevention): NCI research division dedicated to cancer prevention research projects including chemoprevention, nutritional science, genetics, infectious agents, early detection studies, quality of life, and cancer symptom management.

FSRG (Foundations of Science Research Groups): Research groups within the NCI Division of Cancer Prevention (DCP) that focus on scientific aspects of cancer prevention.

MAH (Master Agreement Holder): Pre-approved list of Principle Investigators to whom RFPs are distributed.

OSRG (Organ System Research Groups): Research groups within the NCI Division of Cancer Prevention (DCP) that focus on organ site targeted cancer research studies.

RFP (Request For Proposal): Mechanism used by OSRG to outline the mission for a particular clinical trial. RFPs are distributed to a pre-approved list of Master Agreement Holders (MAH).

TEP (Technical Evaluation Panel): DCP review panel responsible for reviewing clinical research proposals and selecting institutions for contract award.